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Transcutaneous Oxygen Pressure Values Often Fail to Predict Stump Failures after Foot or Limb Amputation in Chronically Ischemic Patients

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Abstract

Objective: Surgeons often recur to Transcutaneous Oxygen Pressure (TCOP) measurements to select the amputation level in patients with critical limb ischemia. Thirty-five mmHg are considered as acceptable threshold for uneventful stump healing.

Methods: Single-centre cohort over 11 years.

Results: We included 303 amputations in 211 adult patients. Forty-two amputations (14%) concerned the mid-foot, 7 (2%) the ankle, 154 (51%) the leg, 28 (9%) the knee joint and 72 (24%) the thigh region. We witnessed 78 stump failures (78/303; 26%) defined as the need for surgical revision or new-level amputation. Our TCOP threshold of 35 mmHg did not discriminate between success and stump failure. Specifically, considering foot and ankle amputations, a 20 mmHg value yielded the same prediction for stump failure as 40 mmHg. The sensitivity, specificity, positive and negative predictive values of a threshold of 35 mmHg for stump failure in foot amputations were 58%, 48%, 56%, and 50%, respectively. The Receiver-Operating-Curve/Area-Under-The-Curve ratio was 0.55. Regarding limb amputations, the threshold of 35 mmHg yielded sensitivity, specificity, positive and negative predictive values of 64%, 51%, 83%, and 28%, respectively. In multivariate analysis adjusting for case-mix, TCOP values were unrelated to stump failure, except for thigh amputations.

Conclusion: For foot and limb amputations, TCOP may confirm clinical impression but does not replace it. Surgeons should avoid using them solely to select the level of amputation.

Keywords: Transcutaneous oxygen; Amputation; Chronic ischemia; Epidemiology; Stump

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Introduction

Despite major advances in the field of lower limb revascularisation in patients with Peripheral Arterial Disease (PAD), patients with chronic Critical Limb Ischemia (CLI) often undergo amputation because of uncontrollable pain, necrosis, and infection. These patients have a high incidence of stump hematoma, ischemia and infection [1-3], requiring a stump revision and/or proximalization of the amputation level [4-6]. This often leads to higher costs, prolonged hospital stay and superimposed additional stress on pre-existing cardiopulmonary and renal diseases in a frequently highly co-morbid patient population [7]. Besides the clinical impression and surgical prerequisites such as absence of flexum, skin necrosis, various haemodynamic measurements performed in vascular laboratories have been used to estimate the optimal level of amputation. None of them is superior to others and none of them is particularly recommended. For example, the ankle-brachial index confirms the diagnosis of PAD the ankle and toe pressure values indicate the presence of CLI, but none of these items has been formally validated for the selection of amputation level [8,9].

Established in the 1980's, Transcutaneous Oxygen Pressure (TCOP) is another technique to measure actual tissue oxygenation which is mainly useful as a prognostic measurement of tissue viability. By extrapolation, it is used to estimate the amputation level targeting on the outcome of postoperative cicatrisation [10]. This technique may predict stump failures in patients with CLI with an accuracy of 78% [11], but remain vulnerable to conditions that can alter the oxygen diffusion

across the skin (hyperkeratosis, oedema) and to localization of the electrode [12]. In two prior studies [1,11], we assessed the association of antibiotic use with stump infection and wound dehiscence. In the first study, TCOP and duration of antibiotic administration showed no association with either outcome, but the TCOP analysis was rudimentary [1]. The second study was a sort of meta-analysis of the literature available in 1996 (without own data) highlighting that a minimal threshold of 20 mmHg before amputation was associated with an 80% chance of successful stump healing [13]. In this large 11-year prospective amputation cohort in the 2000's, we re-examine risk factors for stump dehiscence after lower limb amputations with an emphasis on pre-amputation TCOP and other haemodynamic variables. In contrast, we do not perform meta-analysis of other studies [13] and we do not assess the use of TCOP for revascularization purposes [14].

Methods

Setting before the study

The Orthopaedic Service at Geneva University Hospitals has 132 acute care beds. The foot, limb, and calf amputations requiring prosthesis are prospectively assessed. Moreover, our institution runs a clinical pathway for hospitalized diabetic foot infections, which includes a database on past and ongoing episodes [3]. As part of a hospital-wide quality program, individual informed consent is not required from patients in order to be included in the clinical pathway. Many patients also participated in two prospective randomized trials on diabetic foot infections, of which the present work consists of a side study (Ethical Committee 13-178). Physicians of the Angiology Division performed the TCOP measurements as part of their vascular workup in patients with cardiovascular risk factors and lower limb wounds with in patients in supine position [12], with the use of Radiometer Copenhagen TCM4 Tina (Figure 1). The standardized procedure is described in detail in the literature [15], and all measurements in our angiology division are performed according to standard procedures. TCOP measurement lasts for roughly 20 mins to 25 mins and cost 60 Swiss Francs (60 US$). During the vascular workup, the angiologists performed clinical assessment, ankle and toe pressure measurement and Doppler ultrasound scan of lower limb arteries, and optimized the medical treatment. Based on their clinical and haemodynamic assessment, they determined if CLI was present in which case they presented the patient in a multidisciplinary vascular colloquium to discuss endovascular or surgical revascularization. For this study, we used the last TCOP values before amputation and after revascularization, if the revascularization was performed before elective amputation. We did not take into account postsurgical TCOP values [16].

The surgical technique was at the discretion of the surgical team performing the amputation. Specialized nurses and physiotherapy teams assured the postsurgical care, including wound debridement, the use of vacuum-assisted suction devices or local antiseptic agents. Until postoperative day 5, amputated patients received an additional oxygen supply per nasal (2 L/min, FIO2 21%) and pain-control was often managed by femoral catheter nerve blockade. Hyperbaric oxygen therapy (30 seances per cycle) was optional [17], but available in-house.

Objectives, definitions and exclusion criteria

A stump failure was defined as stump ischemic lesions leading to surgical wound revision in the operating theatre or a new and more proximal amputation within a follow-up period of three months, regardless of the wound size. All eligible patients undergoing lower limb amputation from January 2004 to December 2014 were included in a prospective cohort. It was possible for patients to have been included twice, for example in the case of contra lateral limb disease warranting amputation. Indications for amputation included acute and chronic lower limb infections (ranging from extensive diabetic ulcers with failure of medical treatment to overt gas gangrene) as well as severe PAD with chronic critical limb ischemia not amenable to vascular reperfusion or after failed revascularisation intervention. Exclusion criteria were pediatric patients (age <18 years), amputation distal to the trans-metatarsal line, "guillotine" emergency amputations without primary wound closure, amputees without prior TCOP monitoring, or a short follow-up time less than 3 months.

Figure 1: Device for the measurement of transcutaneous oxygen pressure levels (photo).

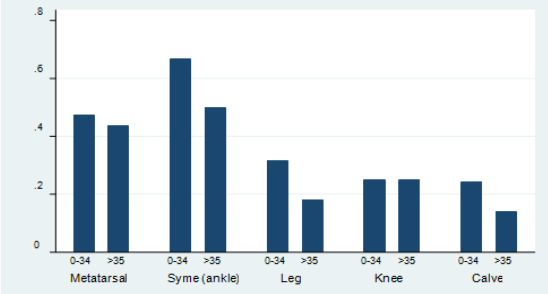

Figure 2: Absolute numbers of stump failures according to amputation level, and stratified between a proximal transcutaneous oxygen pressure level of ≥ 35 mmHg and <35 mmHg.

Statistical analysis

The primary objective was the association of TCOP with stump failure. We also assessed the accuracy of TCOP threshold in predicting stump failure by a ratio of the Receiver-operating-curve/ Area-under-the-curve. Secondary objectives were the determination of other clinical variables associated with that failure. An unmatched logistic regression analysis determined associations with the outcome "stump failure." After first analysing the entire study population, we separately analyzed by stratifying according to the ankle level and a TCOP threshold of 35 mmHg. All analyses were performed separately for the foot, calf and thigh amputation levels. Likewise, we stratified between a value of ≥ 35 mmHg and <35 mmHg. We used STATA™ software (College Station, USA). P values ≤ 0.05 (two-tailed) were significant.

Results

The original prospective cohort study included 303 amputations

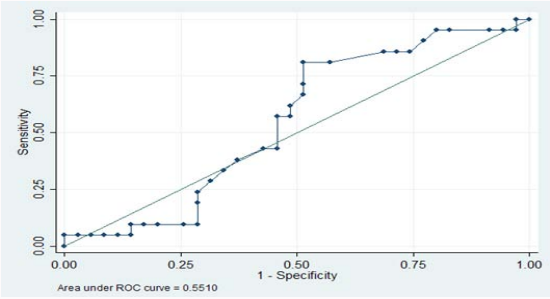

Figure 3: Receiver-operating-curve/Area-under-the-curve ratio for foot amputations.

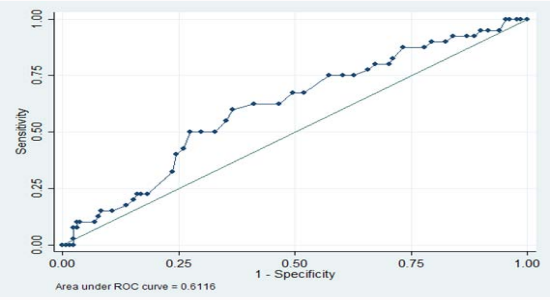

Figure 4: Receiver-operating-curve/Area-under-the-curve ratio for limb amputations.

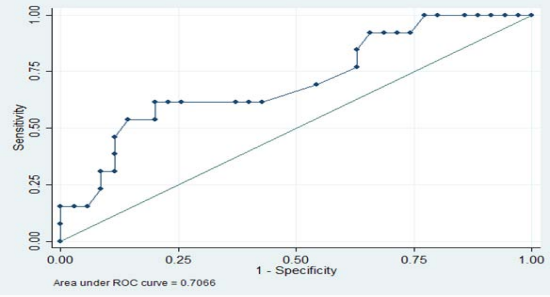

Figure 5: Receiver-operating-curve/Area-under-the-curve ratio for thigh amputations.

in 211 adult patients (73 females; 24%). The median age was 71 years (range, 32-94 years) and the median body mass index 26.4 kg/m2. Half of the patients had diabetes mellitus (156/303; 52%) and the majorities were ever smokers (191; 64%) with a median of 20 UPA. A fifth of all patients (63/303; 21%) showed an American Anesthesiologists' Score (ASA) [18] of 4 points or more; 198 were hypertensive and 165 revealed dyslipidemia. Forty-two amputations (14%) concerned the mid-foot, 7(2%) the ankle, 154 (51%) the leg, 28 (9%) the knee joint and 72 (24%) the thigh region.

We witnessed 78 stump failures (78/303; 26%) that were evenly distributed over the 11-year study period. Our TCOP threshold of 35 mmHg did not differentiate between success and stump failure in various amputation levels (Figure 2). Specifically, considering foot amputations, a 20 mmHg value yielded the same prediction for uneventful stump healing as 40 mmHg. The sensitivity, specificity, positive and negative predictive values of a threshold of 35 mmHg for stump failure in foot amputations were 58%, 48%, 56%, and 50%, respectively. The Receiver-Operating-Curve/Area-Under-The-Curve ratio was 0.55 (Figure 3). Regarding limb amputations, the threshold of 35 mmHg yielded sensitivity, specificity, positive and negative predictive values of 64%, 51%, 83%, and 28%, respectively. Its corresponding Receiver-Operating-Curve/Area-Under-The-Curve ratio was 0.61 (Figure 4). Only for thigh amputations, this ratio was acceptable (0.71; Figure 5).

Multivariate adjustment

Due to differences in crude group comparisons, unmatched logistic regression analyses with the outcome of stump failure were used separately for foot, limb and thigh amputations (Table 1). In all three analyses, TCOP as a continuous variable were unrelated to stump failure, except for thigh amputations. Females tended to have more distal foot amputations, while insulin-dependent patients tended to be more present among the thigh amputees.

Literature search

Our non-systematic literature search selected thirty-one heterogeneous studies investigating the accuracy of TCOP in the prediction of postsurgical success. They mainly stem from the 1980-1990' ties. Their "minimal" threshold of TCOP levels ranges between 10 and 45 mmHg, and some studies failed to define any thresholds (Table 2).

Discussion

We report a high incidence of stump failure (26%; with clinical need for surgical revision/re-amputation) after elective lower extremity amputation in patients with wounds and/or infection and/or necrosis. Hence, our experience reveals more failures than some selected publications advocating 75% [19] or 85% stump healings [19,20]. In the range between 20 and 40 mmHg, compassing the majority of amputees, our pre-operative TCOP measurements did not predict stump failure, except for thigh amputations. Indeed, regarding the foot and limb levels, a TCOP level of 20 mmHg yielded the same prediction as 40 mmHg. Furthermore, in multivariate analyses, there were no formal association between proximal

Table 1: Factors associated with stump failure according to the amputation level.

	Multivariate analysis	Multivariate analysis	Multivariate analysis
	Foot	**Limb**	**Thigh**
Female sex	3.3 (0.6 - 17.1)	1.9 (0.7 - 5.1)	0.1 (0.1 - 4.6)
Insulin-dependent diabetes mellitus	0.6 (0.2 - 2.3)	1.1 (0.5 - 2.5)	11.2 (0.7 - 173.8)
(Ever) smoking	1.0 (0.3 - 3.3)	2.0 (0.8 - 5.0)	0.1 (0.1 - 1.6)
Year of amputation	1.0 (0.8 - 1.2)	1.1 (1.0 - 1.3)	0.8 (0.5 - 1.3)
TCOP [+]	1.0 (1.0 - 1.0)	1.0 (0.9 - 1.0)	0.8 (0.7 - 1.0)

[+] Transcutaneous oxygen pressure as continuous variable
Results are displayed as odds ratio (95% confidence interval).
Variables in bold are statistically significant (two-tailed *p* value <0.05).

Table 2: Selected articles regarding transcutaneous oxygen pressure and stump healing.

Author, year	Number amputations	TCOP threshold*	Prediction of stump healing
Burgess [35]	37	40 mmHg	Above 40 mmHg, all healed
Holstein [36]	102	30 mmHg	Above 30 mmHg, 98% healed
Ito [37]	31	30 mmHg	Above 30 mmHg, 90% healed
Katsamouros [38]	37	22 mmHg	Below 22 mmHg, failure
Ratliff [39]	62	35 mmHg	Above 35 mmHg, all healed
Rhodes [40]	12	25 mmHg	Above 25 mmHg, all healed
Depairon [41]	35	20 mmHg	Above 20 mmHg, 92% healed
Karanfilian [42]	56	10 mmHg	Successful healing >10 mmHg
Dowd [43]	51	40 mmHg	-
Butler [44]	39	40 mmHg	28 (72%) healed
Wyss [10]	206	No threshold	TCOP only of auxiliary help
Wagner [9]	109	No threshold	TCOP only of auxiliary help
Szala [45]	-	40 mmHg	Vascular surgery and amputation mixed
Kram [46]	40	20 mmHg	Above 20 mmHg, 96% healed
Falstie-Jensen [23]	74	No threshold	TCOP of no help
Ameli [47]	38	24 mmHg	-
Lantsberg [48]	24	20 mmHg	All healed
Pinzur [49]	38	30 mmHg	Above 30 mmHg, 92% healed
Bacharach [50]	90	40 mmHg	Positive predictive value 98%;
			<20 mmHg with stump failure
Adera [19]	39	30 mmHg	At 30 mmHg, negative predictive value 90%
Yablon [51]	11	15 mmHg	Below 15mmHg, all stumps failed
Padberg [24]	126	No threshold	Linear associations with healing
Wutschert [11]	615	20 mmHg	Meta-analysis. >20 mmHg, 80% healed
Misuri [52]	30	20 mmHg	Above 20mmHg, 88% healed
Andrews [12]	373	20-40 mmHg	20-40 mmHg range predicts difficulty
Zgonis [53]	35	29 mmHg	Above 29 mmHg, all healed
Poredos [15]	71	none	No thresholds for TCOP
Keyzer [54]	52	30 mmHg	Positive predictive value 41%,
			Negative predictive value 90%
Arsenault [13]	-	20 mmHg	Meta-analysis. Below 20 mmHg failure
Brownrigg [55]	-	25 mmHg	Above 25 mmHg, 25% more healing chance. Meta-analysis of 11 studies
Laroche [29]	-	No threshold	-
Present article	303	No threshold	-

*Threshold of transcutaneous oxygen pressure level identified in the study as predictive of enhanced stump healing

TCOP levels and "stump failure" for amputations below the knee. Finally, receiver-operating-curve and area-under-the-curve analyses ratios were around 50% to 60%, which statistically means quasi equivalence to pure chance. Also existing literature often attributes a decisive threshold for the prediction of stump healing; many studies acknowledge the auxiliary help of TCOP measurements without strict thresholds. According to the studies of the 1980 and 90'ties, acceptable TCPO thresholds may oscillate between 20 mmHg and 45 mmHg [21,22], which correspond perfectly to our "indecisive range". Two meta-analyses equally identify 20 mmHg as a possible minimal threshold, but are not decisive for values above [12,17]. Many trials also failed to determine any thresholds [11,19,23,24], because in everyday's reality, multiple factors influence stump healing; from infection to surgical techniques, hematoma, patient's compliance and more [25]. TCOP are not the only measurement for the selection of amputation levels. The literature is sparse but compares various non-invasive techniques [26]. To cite some examples, Mars et al. compared TCOP with heated and non-heated laser Doppler fluxmetry and attributed an overall accuracy for preoperative prediction of stump healing of 91% [27]. Other prospective studies compared TCOP with the near-infrared spectroscopy versus TCOP [28,29], toe pressure [30], photoplethysmography [31], fluorescein anmgiography [9], skin temperature [9], intradermal xenon [26], transcutaneous carbon dioxide [26], and pressure investigations by laser Doppler [26], which all are considered as possible alternative measurements. Interestingly, the experience of amputation surgeons are not object of scientific evaluation, although in our personal experience, this part is one of the most important ones.

Our Study has Several Limitations

(i) It is retrospective and originates from a single urban institution in a high-income country and excluding toe amputations, which might limit extrapolation of its findings; (ii) We did not control for the degree of lower limb oedema, the use of hyperbaric oxygen [17] and post-amputation mechanical problems. The degree of oedema may significantly vary between the patients, over time, and may significantly influence the actual TCOP levels. Likewise, a deficient surgical technique in the operating theatre such as problems of haemostasis or mechanical problems in the post-surgical period depended on the patient and prosthesis, and may contribute to secondary stump failure [32,33]; (iii) According to real-life situation, we performed TCOP measuring once and by different physicians. The interpersonal and intrapersonal reproducibility of TCOP measurements is unknown, but clinical experience and one study suggest a considerable variety [34]. Likewise, we have arbitrarily chosen a cut-off of 35 mmHg for our statistical analysis among a wide range available in literature as shown in our literature research. This cut-off was the most frequent cut-off in available literature; (iv) Although many variables have been accounted for, others remain unanalyzed; e.g. patients' education [4], off-loading and patients' compliance [3]; (v) Stump failure may have been missed in patients who were treated elsewhere after initial surgery. Given, however, that the Geneva University Hospital is the largest and only public hospital in the area, an early occurrence of adverse outcomes; we consider this selection bias as minima; (vi) Our study did not assess the rapidity of stump healing, since we could not perform a Cox regression analysis or time series analysis. In clinical practice, many stump dehiscences may ultimately heal after several weeks or months of wound debridement, off-loading and local care [3]. In our study, stump failure was defined as the surgical indication for stump revision or a second amputation within 3 months after the first amputation intervention. This indication inherently depends on the patience of the surgical team and often remains subjective; at least partially; (vii) Our study has no comparison between the clinical judgment and the TCOP values before amputation. Such direct prospective head-to-head comparison are lacking in the literature to the best of our knowledge.

In conclusion, TCOP measurements before elective foot or limb amputation in adult patients with end-stage chronic ischemia might inadequately predict future stump failures. In our evaluation, their performance was similar to chance, in contrast to thigh amputations where TCOP levels formally predict failures. For foot and limb amputations, TCOP may confirm the clinical impression of experienced healthcare workers and do not replace a complete angiological examination determining the need presence of severe PAD and need for revascularization. Surgeons should avoid to take these values as granted or to use them to select the level of amputation.

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